

**Efficacy of bromocriptine to reduce body temperature in febrile critically-ill adults with acute neurologic disease: an open-label, blinded endpoint, randomized controlled trial**

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## **UNIVERSITY OF CALIFORNIA, SAN FRANCISCO CONSENT TO PARTICIPATE IN A RESEARCH STUDY**

**Study Title: Efficacy of bromocriptine to reduce body temperature in febrile critically-ill adults with acute neurologic disease: an open-label, blinded endpoint, randomized controlled trial**

This is a medical research study. Dr. Judy Ch'ang, MD, Kristin Slown, PharmD, Michael Trillanes, PharmD, Melissa Nguyen, PharmD, or another member of the research team, will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you are currently in one of the adult Neuro Intensive Care Units (ICU) as you have had an acute brain injury AND you may develop a body temperature or fever (greater than or equal to 38.3°C/ 101°F) due to your brain injury. The study's purpose is to learn if a new approach to lowering your temperature with a drug called "bromocriptine" compared to current treatments may reduce the impact of fever in persons with acute brain injury. Bromocriptine has not been approved by the Federal Food and Drug Administration (FDA) for this use.

If you are the Legally Authorized Representative, the person you are representing is being asked to participate in a research study but is unable to consider whether to give consent to participate because of their medical condition. You, as the patient's legally authorized representative, are being asked to consider whether to give consent for the patient to participate in this study.

### **Why is this study being done?**

The purpose of this study is to see if bromocriptine (Parlodel®) has an effect on you and your body temperature when you have a fever. In this study, you will get either acetaminophen (Tylenol®) OR acetaminophen and bromocriptine only if your body temperature becomes greater than or equal to 38.3 °C (101°F).

### **How many people will take part in this study?**

About 60 intensive care unit patients will take part in this study.

### **What will happen if I take part in this research study?**

If you choose to take part in this study, the following procedures will occur:

If your body temperature rises to 38.3°C or 101°F, you will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor the research team can choose the group you will be in. You will have an equal chance of being placed in any group.

While being in the neuro intensive care unit, if you maintain a temperature less than 38.3°C or 101°F, then you will never be randomized to receive these study medications. After the trial period is over, other clinical data such as laboratory results, antibiotic use or total days spent in the ICU will be obtained through chart review for analysis.

- **If you are in Group 1**

- You will receive a tablet of acetaminophen 650mg by mouth (or per nasogastric or feeding tube if appropriate) every 4 hours for the next 48 hours
- During the 48-hour study period other measures to reduce body temperature such as fans, ice packs, and cooling blankets are not permitted unless a study participant's body temperature is  $\geq 104^{\circ}\text{F}$  ( $40^{\circ}\text{C}$ ).
- The research team member will gather demographic information from your hospital medical record such as your age, gender, ethnicity, and clinical information about your medical diagnosis, acuity, medications, imaging results and laboratory tests.
- If your temperature increases to greater than or equal to  $40^{\circ}\text{C}$  ( $104^{\circ}\text{F}$ ) during the 48-hour study period, your physician will be notified.
- With a continuous temperature probe, temperature will be recorded every 3 seconds. Heart rate and blood pressure will be recorded every 3 seconds if there is an arterial line. If there is no temperature probe or arterial line, vital signs will be recorded at the frequency requested by the treating team.

- **If you are in Group 2**

- You will receive a tablet of acetaminophen 650mg every 4 hours and bromocriptine 5mg every 4 hours by mouth (or per nasogastric or feeding tube if appropriate) for the next 48 hours
- During the 48-hour study period other measures to reduce body temperature such as fans, ice packs, and cooling blankets are not permitted unless a study participant's body temperature is  $\geq 104^{\circ}\text{F}$  ( $40^{\circ}\text{C}$ ).
- The research team member will gather demographic information from your hospital medical record such as your age, gender, ethnicity, and clinical information about your medical diagnosis, acuity, medications, imaging results and laboratory tests.
- If your temperature increases to greater than or equal to  $40^{\circ}\text{C}$  ( $104^{\circ}\text{F}$ ) during the 48-hour study period, your physician will be notified.
- With a continuous temperature probe, temperature will be recorded every 3 seconds. Heart rate and blood pressure will be recorded every 3 seconds if there is an arterial line. If there is no temperature probe or arterial line, vital signs will be recorded at the frequency requested by the treating team.

After 30 days, you will be contacted by a research team member for a follow up phone call which should take approximately 15 minutes. If you are unable to complete the phone assessment, your surrogate, family member, friend, legally authorized representative, nursing staff, physician or medical healthcare professional taking care of you may answer on your behalf.

**Study location:** All study activities will be done in your room in one of the adult ICUs at UCSF

## Medical Center or Zuckerberg San Francisco General Hospital and Trauma Center

### **How long will I be in the study?**

Participation in the study will take a total of about 48 hours during your ICU stay. Then 30 days later, you or your surrogate will be contacted by a research team member for a follow up phone call which should take approximately 15 minutes.

### **Can I stop being in the study?**

Yes. You can decide to stop at any time. Tell the research team member if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely. The research team member may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

### **What side effects or risks can I expect from being in the study?**

You may have side effects while in the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking acetaminophen or bromocriptine. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your research team member about any side effects that you experience while taking part in the study.

During each nursing shift throughout the 48-hour study period, from the first time you received a study drug, the bedside nurse will do a 5-minute assessment to monitor for any side effects from the study medications.

### **Risks and side effects related to the drug include those which are:**

#### **Likely**

- none

#### **Less Likely**

- fatigue
- nausea
- headache
- hypotension
- dizziness
- abdominal cramps
- constipation
- drowsiness

#### **Rare but serious**

- gastrointestinal bleeding
- hypertension
- psychosis
- seizure, stroke, heart attacks (especially in women in the postpartum period)
- arrhythmia or abnormal heart rhythm (seen mostly in patients with history of acromegaly which is a hormonal disorder that develops when your pituitary gland produces too much growth hormone during adulthood.)

**Randomization risks:** You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

**Unknown Risks:** The experimental treatment may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your research team member.

### **Are there benefits to taking part in the study?**

Taking part in this study may or may not make your health better. While doctors hope that the addition of the drug, bromocriptine, will be more effective than the standard or usual treatment (acetaminophen alone), there is no proof of this yet.

There will be no direct benefit to you from participating in this study. However, this study will help doctors and nurses learn more about bromocriptine, and it is hoped that this information will help in the treatment of future ICU patients with acute brain injury who have fever.

### **What other choices do I have if I do not take part in this study?**

Your other choices may include:

- Getting no treatment
- Getting standard treatment for your condition without being in a study
- Getting a different experimental treatment/taking part in another study.

Please talk to your doctor about your choices before deciding if you will take part in this study.

### **Will my medical information be kept private?**

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The University of California
- Other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other health care providers may see your test results and become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

### **What are the costs of taking part in this study?**

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network. Any procedures done only for research will not be charged to you or your insurer. The trial itself will provide the drug, bromocriptine, and administration of bromocriptine will be at no cost to you.

### **Will I be paid for taking part in this study?**

You will not be paid for taking part in this study.

### **What happens if I am injured because I took part in this study?**

It is important that you tell your research team member, Dr. Judy Ch'ang, MD, Kristin Slown, PharmD, Michael Trillanes, PharmD, or Melissa Nguyen, PharmD if you feel that you have been injured because of taking part in this study. You can tell the researcher in person or call her/him at 415-514-2120 or 415-206-8094.

**Treatment and Compensation for Injury:** If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

### **What are my rights if I take part in this study?**

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or

your willingness to continue in the study. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

### **Who can answer my questions about the study?**

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your research team members(s) Judy Ch'ang, MD, Kristin Slown, PharmD, Michael Trillanes, PharmD or Melissa Nguyen, PharmD at 415-514-2120 or 415-206-8094.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Institutional Review Board at 415-476-1814. A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

### **CONSENT**

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

**PARTICIPATION IN RESEARCH IS VOLUNTARY.** You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

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Date

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Participant's Signature for Consent

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Date

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Person Obtaining Consent

**AND/OR**

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Date

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Legally Authorized Representative

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Date

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Person Obtaining Consent

**Participant consent after legally authorized representative consent was obtained:**

You were enrolled in this study by a surrogate because your illness rendered you incapable of providing informed consent when you were initially enrolled. You have since regained your ability to provide consent and now would like to:

\_\_\_\_\_ Continue participation until the study is complete (if applicable)

\_\_\_\_\_ Terminate your participation in the study but allow the use of data collected to date

\_\_\_\_\_ Terminate your participation in the study and not allow use of data collected to date

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Date

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Participant's Signature for Consent

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Date

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Person Obtaining Consent